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Original Article

Protective Effects of *Aju Mbaise* Extract against Dutasteride-Induced Biochemical and Haematological Changes in Rats

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Abstract

Background and Aim: *Aju Mbaise* is a nutraceutical food supplement taken by nursing mothers within their first three months of delivery due to its health advantages. This study evaluated the protective potentials of *Aju Mbaise* extract on the renal functions, lipid profile, and haematological indices of Dutasteride-induced rats.

Materials and Methods: This study had sham control, dutasteride control, an extract group that received 1000 *mg/kg of Aju Mbaise* only, and Dutasteride induced groups treated with 500 and 1000 *mg/kg of Aju Mbaise* orally for 28 consecutive days.

Results: Dutasteride induction caused a remarkable increase in the serum urea, creatinine, sodium, potassium, and chloride ions and a considerable reduction in the serum bicarbonate ions in the Dutasteride control compared to the sham control. The lipid profile indicated a significant increase in the total serum cholesterol, triacylglycerol, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol, along with a substantial decline in the serum high-density lipoprotein cholesterol of the Dutasteride control relative to the sham control. The haematological parameters, including red blood cell, packed cell volume, haemoglobin, mean corpuscular haemoglobin concentration, and neutrophils, decreased significantly in the Dutasteride control relative to the sham control. In contrast, the Dutasteride control showed a significant increase in the mean corpuscular volume, white blood cell, platelet, and lymphocyte counts compared to the sham control. The treatment of Dutasteride-induced rats with 500 and 1000 *mg/kg* of *Aju Mbaise* extract significantly restored the serum urea, creatinine, serum electrolytes, lipid profile, and haematological parameters to normal levels compared to the Dutasteride control. None the rats had any observable alteration in the kidney histo-architecture.

Conclusion: Our findings showed that *Aju Mbaise* extract could attenuate changes in renal functions, lipid profile, and haematological indices associated with Dutasteride toxicity in rats.

Keywords: *Aju Mbaise***,** Dutasteride toxicity, Renal function, Lipid profile, Haematological indices

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Introduction

Renal disease is one of the most common causes of death globally. Renal replacement is the only viable treatment option and requires efforts to manage or prevent its occurrence (1). Many unhealthy alterations of haematological and biochemical functions, including kidney functions, lipid profile, antioxidants, and impaired liver functions, are associated with adverse reactions emanating from the consumption of some therapeutic drugs, herbal medicines toxins, and both persistent and non-persistent environmental pollutants. Renal injury or impairment of renal functions is caused mainly by the effects of relentless oxidative stress and increased lipid peroxidation levels, as evidenced in the cases of acetaminophen and carbon tetrachloride (2, 3). In renal disease, the decline in the number of functional nephrons coupled with the reduction in the glomerular filtration rate gives rise to excess ammonium ions in the body, which causes metabolic acidosis because of the elevated hydrogen ion concentration (4). The decline in serum electrolyte levels, including bicarbonate ions, and elevated sodium, potassium, and chloride ion levels are reliable indicators of kidney disorders or diseases that mostly correlate with kidney histology alterations (5, 6). The high cost and health burdens of dialysis and kidney transplants promote interests in medicinal plants research for the formulations of herbal drugs to prevent, treat, and manage kidney diseases (7).

Dyslipidaemia increases the risk of atherosclerosis, stroke, obesity, hypertension, insulin resistance, diabetes, and impairment of renal functions. Various studies have implicated very abnormal lipid profiles as the primary cause of many disorders or disease conditions (8). The low serum HDL level is responsible for most complications related to dyslipidaemia because cholesterol and LDL are deposited on the blood vessels due to the inability of low serum HDL to efficiently transport them to the liver for metabolism (9). Elevated total serum cholesterol and LDL levels increase the risk of coronary heart disease and are responsible for many deaths globally (10, 11). Many plant-derived nutraceuticals that possess lipid-lowering properties are helpful in the prevention and management of heart disease. Those medicinal plants that lower serum LDL concentrations are more effective in reducing the risks of cardiovascular diseases (12, 13). Many studies have reported altered haematological indices in nephropathy associated with impaired erythropoiesis, deformed erythrocytes, shortened erythrocyte half-life, increased anisocytosis, and elevated mean corpuscular volume (14).

Aju Mbaise is a traditional food supplement with nutraceutical properties given to women immediately after childbirth and during the period of nursing the child in Mbaise communities in Imo State, Nigeria, which has gained wide acceptance across south-eastern parts of the country. It is a routine diet for nursing mothers because of its nutraceutical properties that help to flush out unwanted blood and remnants of the placenta and replenishes the blood lost during childbirth. It has a high safety margin, and none of the consumers has reported any adverse reactions or toxicity after its consumption despite being consumed in large volumes for the first three after delivery. *Aju Mbaise* is a mixture of six different therapeutic plants, including *Spondias mombine, Uvaria chamae*, *Napoleona vogelli*, *Ceiba petandra*, *Euphorbia convolvuloids*, and *Barteria fistulosa*, which contribute to its overall nutraceutical properties (15, 16). Literature surveys show that it is a good source of vitamins, proteins, phytochemicals, and other micronutrients that could promote optimum body functions (17). It alleviates pains, induces normal menstrual flow, sanitizes the womb after delivery or miscarriage, prevents infections, and has been shown to possess antimalarial, anti-inflammatory, and antitumor properties, as reported in traditional medicine (18). It promotes ovulation and fertility in women of childbearing age and enhances lactation (16). It contains substantial amounts of alkaloids, flavonoids, glycosides, phenols, tannins, and terpenoids, and low amounts of hydrogen cyanides, saponins, and steroids for its pharmacological activities (18). Polyherbal extracts are safer and therapeutically more effective than any individual plant (19). Having seen the enormous medicinal potential of Aju Mbaise, the present study examined the protective effects of *Aju Mbaise* extract against Dutasteride-induced biochemical and haematological changes in rats.

Materials and Methods

Experimental Animals

The present study used thirty male Wistar albino rats weighing 160-170 g. The rats were obtained from the Animal Production Unit of the College of Biological Sciences, University of Nigeria Nsukka, Nigeria. They were allowed to adapt to the new environment at the Animal House of the College of Natural Sciences, Michael Okpara University of Agriculture Umudike, with unhindered access to standard animal feed and drinking water. We handled the rats according to the guidelines in the ethical approval for the study. The approval for the study was issued by the Ethical Committee of the Department of Physiology, Biochemistry, and Pharmacology, Michael Okpara University of Agriculture, Umudike (MOUAU/VPP/EC/18/005).

Chemicals and Drugs

We obtained the Dutasteride drug to induce toxicity in rats from the GlaxoSmithKline group of companies, United Kingdom. Analytical grade ethanol and chloroform purchased from Sigma-Aldrich Chemicals, United States, were used to extract plant materials and anaesthetize the rats.

Preparation of *Aju Mbaise* Extract

The *Aju Mbaise* samples obtained from Mbaise, Imo State, Nigeria, were sliced into smaller sizes and dried under a controlled temperature for four weeks to attain a constant dry weight before being ground into a coarse powder. A quantity of 1000 g of the ground sample was macerated in 3.0 L absolute cold ethanol (98 % L) for three days with intermittent shaking, followed by filtration with a Whatman No. 1 filter paper. The filtrate was concentrated with a rotary evaporator to obtain a gel-like extract, with a percentage yield of 16.32 %, corresponding to 163.2 g.

Experimental Design

This study was conducted using five groups of rats, each containg six animals, including the sham control (without Dutasteride induction), Dutasteride control (0.5 mg/kg only), rats administered 1000 *mg/kg of Aju Mbaise* extract only, Dutasteride-induced rats+500 *mg/kg of Aju Mbaise* extract, and Dutasteride-induced rats+1000 *mg/kg of Aju Mbaise* extract. The rats were orally administered 0.5 mg/kg of Dutasteride, and Aju Mbaise extracts for 28 consecutive days after an hour. After 28 days, the rats were fasted overnight and anaesthetized with chloroform on the 29th day. Then, blood samples were gathered from the rats through cardiac puncture for haematological, serum electrolyte, urea, creatinine, and lipid profile analyses. At the same time, kidneys were harvested from the rats for histological examination.

Haematological Analyses

The haematological parameters including red blood cells (RBC), packed cell volume (PCV), haemoglobin (Hb), white blood cell (WBC), platelets, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and mean corpuscular haemoglobin (MCH), were determined using previous reported methods (20, 21).

Determination of Renal Function Parameters

The serum urea, creatinine, and electrolytes, including sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate ion concentrations, were determined according to the procedures outlined in its respective Randox assay kits.

Determination of the Lipid Profile

The serum cholesterol, and triacylglycerol (TAG), were determined by the methods of Albers *et al*. (22). The high-density lipoprotein cholesterol (HDL-C) concentrations were quantified according to the procedures outlined by Allain *et al*. (23). The low-density lipoprotein cholesterol (LDL-C) and very-low-density lipoprotein cholesterol (VLDL-C) were calculated using the equations outlined by Friedelwald *et al.* (24).

Histopathological Examination of Kidney Tissues

The harvested kidney tissues were fixed in 10% formalin followed by paraffin wax. Subsequently, they were dehydrated and stained with haematoxylin and eosin dyes. They were further processed, and the histopathological changes were examined in a microscope, as earlier outlined by Uroko *et al*. (25).

Data Analysis

The data obtained were statistically analysed with one-way analysis of variance (ANOVA), including least significant difference (LSD) and Duncan multiple comparison test using a Statistical Product and Service Solutions (SPSS) version 22 and statistical significance established at $P<0.05$.

Results and Discussion

Effects of *Aju Mbaise* Extract on the Renal Function Parameters of the Rats Undegoing Toxicity Induced by Dutasteride

The Dutasteride control and Dutasteride+500 mg/kg of *Aju Mbaise* extract demonstrated a significant elevation in the serum urea concentrations compared with the sham control and Dutasteride+1000 mg/kg of *Aju Mbaise* extract, respectively (Table 1). The rats administered with 1000 mg/kg of *Aju Mbaise* extract only and Dutasteride-induced rats treated with *Aju Mbaise* extract exhibited a remarkable decline in the serum urea concentrations relative to the rats administered Dutasteride control.

The serum creatinine concentrations in Table 1 displayed a significant increase in the dutasteride control and Dutasteride-induced rats treated with *Aju Mbaise* extract compared to the sham control and rats that received only 1000 mg/kg of *Aju Mbaise* extract. In contrast, the rats administered with 1000 *mg/kg of Aju Mbaise* extract only and Dutasteride-induced rats treated with 500 and 1000 mg/kg of *Aju Mbaise* extract showed a significant decrease in the serum creatinine levels compared with the dutasteride control.

The serum Na^+ and Cl^- ions indicated a significant increase in the Dutasteride control and Dutasteride-induced rats treated with 500 and 1000 mg/kg of *Aju Mbaise* extract compared to the sham control and rats administered with 1000 mg/kg of *Aju Mbaise* extract only, respectively (Table 1). Besides, the Dutasteride-induced rats treated with *Aju Mbaise* extract and normal rats administered 1000 *mg/kg of Aju Mbaise* extract demonstrated a noticeable reduction in the serum Na^+ and Cl^- levels compared with the Dutasteride-induced untreated rats.

The serum K^+ ions showed a significant rise in the Dutasteride control and Dutasteride-induced rats treated with 500 mg/kg of *Aju Mbaise* extract relatively to the sham control and Dutasteride-induced rats treated with 1000 mg/kg of *Aju Mbaise* extract, respectively (Table 1). Still, the serum K^+ levels showed a significant decrease in the rats administered with only 1000 mg/kg of Aju Mbaise extract, Dutasteride+500 mg/kg of Aju Mbaise extract, and Dutasteride+1000 mg/kg of *Aju Mbaise* extract compared with the Dutasteride control.

Table 1 indicates a significant reduction in the serum bicarbonate levels of the Dutasteride control, Dutasteride-induced rats treated with 500 and 1000 mg/kg of *Aju Mbaise* extract compared with the sham control and rats that received 1000 *mg/kg of Aju Mbaise* extract only, respectively. The bicarbonate levels of the Dutasteride-induced rats treated with 500 and 1000 mg/kg of *Aju Mbaise* extract were significantly elevated relative to the Dutasteride control.

Values show the mean ± standard deviation (n = 5), and with a different letter, superscripts are significantly different ($P<0.05$) from any paired mean across the row.

Effects of *Aju Mbaise* Extract on the Lipid Profile of the Rats Undergoing Toxicity with Dutasteride

The total serum cholesterol levels in Table 2 showed that only the Dutasteride control rats had significantly elevated total serum cholesterol levels compared with the sham control. At the same time, the rats

Table 1: Renal Function Parameters of the Rats Undergoing Toxicity with Dutasteride Treated with *Aju Mbaise* Extract.

Parameters	Sham control	Dutasteride control	*Aju Mbaise* (1000 mg/kg)	Dutasteride + 500 *mg/kg of Aju Mbaise*	Dutasteride + 1000 *mg/kg of Aju Mbaise*
Urea (mg/dl)	12.31 ± 0.75^{a}	17.21 ± 1.03^{c}	11.68 ± 1.38^{a}	14.06 ± 0.54^{b}	12.64 ± 0.64^{a}
Creatinine (mg/dl)	0.50 ± 0.04^{a}	0.82 ± 0.03^{d}	0.49 ± 0.03^{a}	0.62 ± 0.02^{c}	0.56 ± 0.05^{b}
Na^+ (mEq/L)	115.20 ± 3.96^{a}	141.20 ± 4.55^{d}	118.40 ± 1.82^{a}	133.60 ± 1.14^{c}	124.80 ± 0.84^{b}
K^+ (mEq/L)	$4.59\pm0.19^{a,b}$	5.94 ± 0.25^{d}	4.44 ± 0.18^{a}	5.13 ± 0.21^{c}	4.76 ± 0.17^{b}
Cl^- (mEq/L)	94.15 ± 1.13^{a}	109.97 ± 3.21^{d}	93.62 ± 2.34^{a}	102.50 ± 0.79^{c}	97.35 ± 1.26^{b}
Bicarbonate (mmol/L)	21.20 ± 0.80^{c}	17.66 ± 1.42^{a}	22.82 ± 0.78^{c}	19.22 ± 0.26^{b}	19.96 ± 0.76^{b}

administered only 1000 mg/kg of *Aju Mbaise* extract and Dutasteride-induced rats treated with 500 and 1000 mg/kg of *Aju Mbaise* extract, respectively, exhibited significantly reduced total serum cholesterol levels in comparison with the dutasteride control rats. Table 2 indicates a significant decline in the HDL-C of the Dutasteride control and the Dutasteride-induced rats treated with 500 *mg/kg of Aju Mbaise* extract compared with the sham control. Still, no remarkable difference was observed between the serum HDL-C level in the rats administered with only 1000 *mg/kg of Aju* Mbaise extract and Dutasteride-induced rats treated with 1000 *mg/kg of Aju Mbaise* extract relative to the sham control. However, the rats that received only 1000 *mg/kg of Aju Mbaise* extract and Dutasteride-induced rats treated with *Aju Mbaise* extract had significantly elevated serum HDL-C levels compared with the dutasteride control rats.

The serum TAG concentrations of the Dutasteride-induced untreated rats were significantly higher than the sham control (Table 2). On the hand, the serum TAG levels in the rats administered with only 1000 *mg/kg of Aju Mbaise* extract and Dutasteride -induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract declined significantly compared with the sham control and dutasteride control rats, respectively.

A significant increase was observed in the serum low-density lipoprotein-cholesterol (LDL-C) of the Dutasteride-induced untreated rats and Dutasteride-induced rats treated with 500 *mg/kg of Aju Mbaise* extract relative to the sham control. Besides, there was a significant decrease in the serum LDL-C levels in the rats administered with 1000 *mg/kg of Aju Mbaise* extract and all the Dutasteride-induced rats treated with *Aju Mbaise* extract compared with the Dutasteride-induced rats.

Table 2 shows significantly high levels of very low-density lipoprotein-cholesterol (VLDL-C) levels in the Dutasteride control compared with the sham control. Conversely, there was no significant decrease in the serum VLDL-C levels of the administered 1000 *mg/kg of Aju Mbaise* extract compared with the Dutasteride control. The Dutasteride-induced rats treated with *Aju Mbaise* extract showed substantial reductions in the serum VLDL-C concentrations compared with the sham control and dutasteride control rats, respectively.

Values show the mean ± standard deviation (n = 5), and with a different letter, superscripts are significantly different (P < 0.05) from any paired mean across the row.

Effects of *Aju Mbaise* Extract on the Haematological Parameters of the Rats Undergoing Toxicity with Dutasteride

The haematological parameters in Table 3 show a significant decline in the Dutasteride control rats' RBC counts, PCV, and Hb concentrations compared with the sham control rats. There were no significant differences in the RBC count, PCV, and Hb concentrations of the rats administered with only 1000 *mg/kg of Aju Mbaise* extract relative to the sham control. The Dutasteride -induced rats treated with 500 *mg/kg of Aju Mbaise* extract showed a significant reduction in the RBC counts, PCV, and Hb concentration compared with the sham control but significantly high relative to the dutasteride control rats. Moreover, the RBC counts, PCV, and Hb concentrations of the Dutasteride-induced rats treated with 1000 *mg/kg of Aju Mbaise* extract were noticeably higher compared with the Dutasteride control rats.

Table 2: Lipid Profile Parameter Concentrations in the Rats Undergoing Toxicity with Dutasteride Treated with *Aju Mbaise* Extract.

Parameters	Sham control	Dutasteride control	*Aju Mbaise* (1000 mg/kg)	Dutasteride + 500 *mg/kg of Aju Mbaise*	Dutasteride + 1000 *mg/kg of Aju Mbaise*
Cholesterol (mg/dl)	60.37 ± 3.05^{a}	82.92 ± 2.01^{b}	60.20 ± 1.21^{a}	63.45 ± 1.77^{a}	59.15 ± 1.24^{a}
HDL-C (mg/dl)	31.03 ± 2.87^{c}	21.19 ± 0.90^{a}	32.97 ± 1.08^{c}	27.80 ± 1.83^{b}	33.61 ± 1.12^{c}
TAG (mg/dl)	69.32 ± 2.15^{b}	85.82 ± 1.31^{c}	63.14 ± 4.24^{a}	65.56 ± 2.16^{a}	65.22 ± 2.48^{a}
LDL-C (mg/dl)	15.19 ± 4.78^{a}	44.57 ± 2.40^{c}	14.61 ± 1.86^{a}	22.53 ± 2.26^{b}	12.49 ± 1.31^{a}
VLDL-C (mg/dl)	13.86 ± 0.43^{b}	17.16 ± 0.26^{c}	12.63 ± 0.85^{a}	13.11 ± 0.43^{a}	13.04 ± 0.50^{a}

Values show the mean ± standard deviation (n = 5), and with a different letter, superscripts are significantly different (P < 0.05) from any paired mean across the row.

The WBC counts of the Dutasteride control rats exhibited a significant increase relative to the sham control (Table 3). However, the rats that received only 1000 mg/kg of Aju Mbaise extract and Dutasteride-induced rats treated with 1000 *mg/kg of Aju Mbaise* extract demonstrated a remarkable decline in the WBC counts compared to the sham control and Dutasteride control rats, respectively. No significant difference was observed between the WBC counts of the Dutasteride-induced rats treated with 500 *mg/kg of Aju Mbaise* extract and the sham control. Still, the WBC counts of the Dutasteride-induced rats treated with 500 *mg/kg of Aju Mbaise* extract were significantly decreased compared with the dutasteride control rats.

The platelet counts of Dutasteride-induced untreated rats increased significantly relative to the sham control (Table 3). Contrarily, there were no significant variations in the platelet counts of the rats administered 1000 *mg/kg of Aju Mbaise* extract and all the Dutasteride-induced rats treated with *Aju Mbaise* extract compared to the sham control. However, all the Dutasteride-induced rats treated with *Aju Mbaise* extract significantly declined platelet counts compared with Dutasteride-induced untreated rats.

The results in Table 3 show a noticeable decline in the MCV levels of the Dutasteride-induced untreated rats and rats administered 500 mg/kg of *Aju Mbaise* extract compared with the sham control. However, there were no significant variations in the MCV levels of all the Dutasteride-induced rats treated with *Aju Mbaise* extract in comparison with the sham control and Dutasteride-induced untreated rats.

No significant difference was observed in the MCH levels of the rats administered with 1000 *mg/kg of Aju Mbaise* extract only, dutasteride control rats, and Dutasteride induced rats treated with *Aju Mbaise* extract compared with the sham control rats (Table 3). In contrast, the rats administered 1000 mg/kg of *Aju Mbaise* extract only had a significantly elevated MCH level in comparison the dutasteride control rats.

The MCHC concentration of the Dutasteride control rats declined significantly compared with the sham control (Table 3), while there was no significant decline in the MCHC concentrations of the rats administered with only 1000 mg/kg of *Aju Mbaise* extract, and

Table 3: Haematological Parameters of the Rats Unergoing Toxicity with Dutasteride Treated with *Aju Mbaise* Extract.

Parameters	Sham control	Dutasteride control	*Aju Mbaise* (1000 mg/kg)	Dutasteride + 500 mg/kg*Aju Mbaise*	Dutasteride + 1000 *mg/kg of Aju Mbaise*
RBC ($x10^6/mm^3$)	7.92 ± 0.21^{c}	5.95 ± 0.74^{a}	7.65 ± 0.15^{c}	7.00 ± 0.41^{b}	$7.53\pm0.16^{b,c}$
PCV (%)	49.40 ± 1.14^{c}	40.40 ± 2.07^{a}	53.00 ± 1.58^{d}	45.00 ± 2.55^{b}	50.20 ± 2.39^{c}
Hb (g/dl)	17.52 ± 0.36^{d}	11.86 ± 0.92^{a}	17.66 ± 0.67^{d}	14.40 ± 0.81^{b}	16.48 ± 0.57^{c}
WBC ($x10^3/mm^3$)	10.00 ± 0.23^{b}	18.24 ± 0.50^{c}	8.82 ± 0.82^{a}	10.14 ± 0.26^{b}	9.10 ± 0.52^{a}
Platelets ($x10^3/mm^3$)	131.80 ± 3.77^{a}	158.40 ± 5.60^{b}	129.40 ± 3.05^{a}	128.40 ± 2.97^{a}	128.20 ± 1.79^{a}
MCV (pg)	62.40 ± 2.56^{a}	68.64 ± 8.26^{b}	69.27 ± 2.71^{b}	$64.30\pm2.22^{a,b}$	$66.66\pm1.83^{a,b}$
MCH (fl)	$22.12\pm0.46^{a,b}$	20.16 ± 2.81^{a}	23.08 ± 0.92^{b}	20.63 ± 1.86^{a}	$21.90\pm0.81^{a,b}$
MCHC (g/dl)	35.49 ± 1.48^{b}	29.45 ± 3.10^{a}	33.34 ± 1.62^{b}	$32.13\pm3.23^{a,b}$	32.88 ± 1.79^{b}
Neutrophils (%)	29.4 ± 2.37^{b}	24.2 ± 4.42^{a}	34.0 ± 5.23^{b}	33.0 ± 5.23^{b}	32.0 ± 5.23^{b}
Lymphocytes (%)	56.1 ± 2.64^{a}	60.9 ± 2.55^{b}	54.3 ± 5.23^{a}	49.3 ± 5.23^{a}	53.3 ± 5.23^{a}
Monocytes (%)	8.9 ± 1.60^{a}	8.4 ± 2.35^{a}	8.8 ± 2.71^{a}	7.8 ± 2.71^{a}	8.6 ± 2.71^{a}
Eosinophils (%)	2.6 ± 0.53^{a}	2.8 ± 0.63^{a}	2.5 ± 0.68^{a}	2.3 ± 0.68^{a}	2.1 ± 0.68^{a}

Values show the mean ± standard deviation (n = 5), and with a different letter, superscripts are significantly different ($P < 0.05$) from any paired mean across the row.

Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract, respectively, compared with the sham control. In contrast, the rats administered with only 1000 *mg/kg of Aju Mbaise* extract and Dutasteride-induced rats treated with 1000 *mg/kg of Aju Mbaise* extract exhibited a significant rise in the MCHC concentrations in comparison with the dutasteride control.

The neutrophil counts in Table 3 indicated a significant rise in the Dutasteride-induced untreated rats compared with the sham control. There was no significant difference in the neutrophil counts of the rats administered with 1000 *mg/kg of Aju Mbaise* extract only and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract compared with the sham control, respectively. On the other hand, there was a significant increase in the neutrophil counts of the rats administered 1000 *mg/kg of Aju Mbaise* extract only and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract, respectively, compared with the dutasteride control rats.

The data in Table 3 displayed a significant increase in the lymphocyte counts of the Dutasteride-induced untreated rats compared with the sham control. Moreover, there were no substantial changes in the lymphocyte counts of rats administered witth only 1000 *mg/kg of Aju Mbaise* extract and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract compared with the sham control. Contrarily, the Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract had significantly diminished lymphocyte counts compared to the Dutasteride-induced untreated rats.

Table 3 indicated no significant variations in the percentage of monocytes and eosinophils of the dutasteride-control, rats administered with 1000 *mg/kg of Aju Mbaise* extract only, and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract, respectively compared with the sham

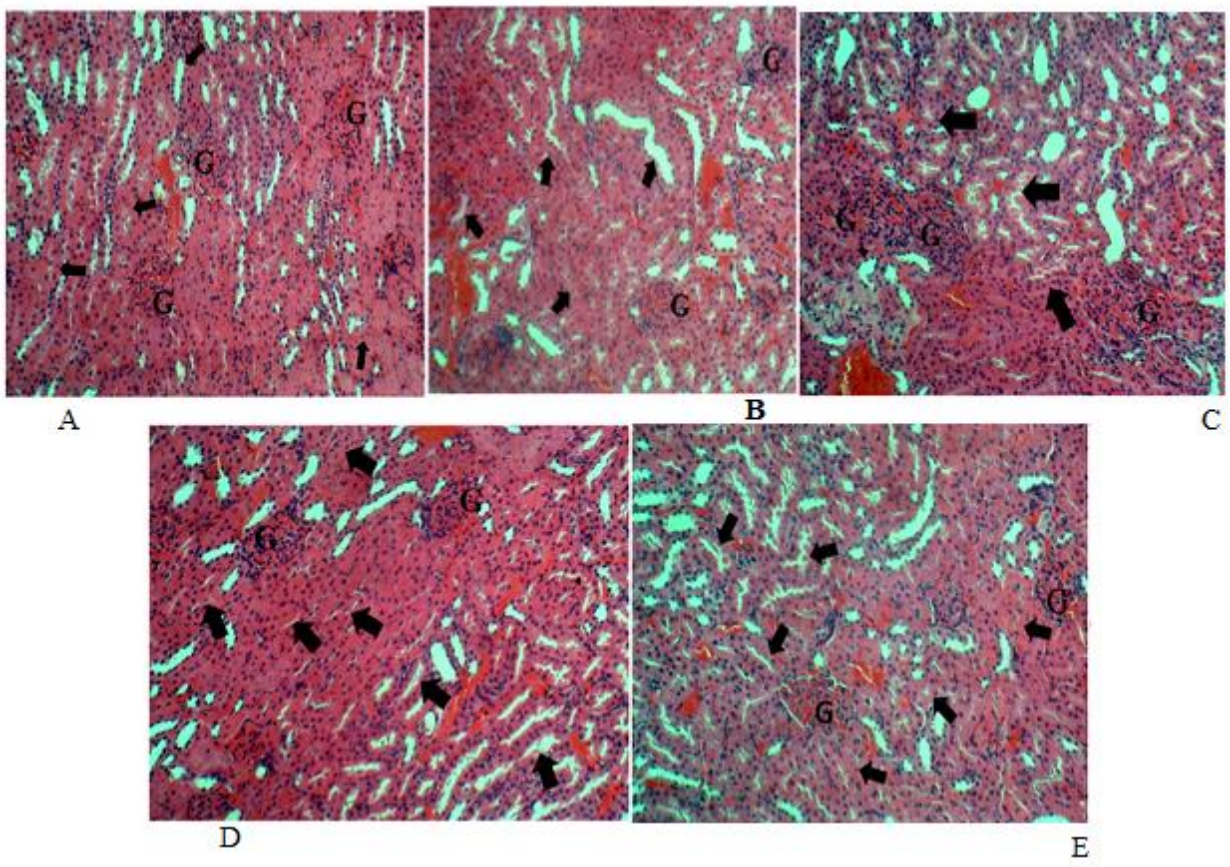

Figure 1. 1A-1E are the photomicrographs of kidney sections of rats from the sham control, Dutasteride control, *Aju Mbaise* extract (1000 mg/kg), Dutasteride+*Aju Mbaise* extract (500 mg/kg), and Dutasteride+*Aju Mbaise* extract (1000 mg/kg), respectively.

control rats. Similarly, the rats administered with 1000 *mg/kg of Aju Mbaise* extract only and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract, respectively, exhibited no significant changes in the monocyte and eosinophil counts relative to the dutasteride control rats.

Values show the mean ± standard deviation (n = 5), and with a different letter, superscripts are significantly different ($P < 0.05$) from any paired mean across the row.

Photomicrographs of Kidney Sections from Dutasteride-Treated Rats Treated with theEthanol Extract of *Aju Mbaise*

Sections of the kidney presented in Figure 1 A-1 E showed normal renal histomorphology with normal glomeruli (G) in their bowman's capsules and normal renal tubules (arrow).

teride. Dutasteride is a therapeutic drug for managing benign prostatic hyperplasia in ageing men. Still, many adverse side effects, including impairment of renal function, liver injury, shrinking testes, low libido, erectile malfunction, diabetes, and metabolic syndromes (26, 27, 28) have been observed. Although Dutasteride mediates its therapeutic effects by inhibiting a 5α-reductase enzyme activity critical in converting testosterone to dihydrotestosterone, the toxicity profile of Dutasteride is not fully understood. The significantly elevated serum urea and creatinine levels in the Dutasteride control rats showed impaired glomerular filtration rate, suggesting that the Dutasteride induction caused a decline in renal function in line with the previous findings (29). The changes in the serum urea and creatinine levels are reliable indicators of renal function status. Their stories are usually low in a normal healthy, functional kidney due to high glomerular filtration rate and rapid clearance. Still, their concentrations get elevated in damaged kidneys or compromise renal functions. Dutasteride induction may have caused kidney damage or inflammation that resulted in the reduced creatinine filtration of the glomerular and decreased rate of excretion through urine.

In contrast, the low serum urea and creatinine levels in the rats that received 1000 *mg/kg of Aju Mbaise* extract revealed that rats could maintain normal kidney functions, including urea and creatinine filtration and clearance. The normal kidney functions in the rats administered with 1000 *mg/kg of Aju Mbaise* extract only indicated that *Aju Mbaise* extract possesses no nephrotoxic effects; instead, it could confer nephroprotective effects. The dose-dependent significant decline in the serum urea and creatinine concentrations in the Dutasteride -induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract, respectively, relative to the dutasteride control rats, are attributed to the nephroprotective property of the *Aju Mbaise* extract. This finding is consistent with the findings of Rajakrishnan *et al*. (30). The effects of *Aju Mbaise* extract on the serum urea and creatinine concentrations of Dutasteride-induced rats showed that *Aju Mbaise* extract could exhibit high nephroprotective activity at an increased dose. The 1000 mg/kg of *Aju Mbaise* administered reversed the elevated serum urea levels in the Dutasteride-induced rats to an average level and creatinine level to a near normal. These decreases in the serum urea and creatinine levels in the Dutasteride-induced rats treated with *Aju Mbaise* extract showed that *Aju Mbaise* extract was able to restore normal renal functions in the rats, which enabled the effective filtration of urea and creatinine by the glomerular of the kidney and promoted their rapid excretion from the urine (29).

Healthy kidneys play a vital role in maintaining adequate electrolyte balance, including potassium, sodium, chloride, and bicarbonate ion levels in the blood, to ensure normal biochemical and physiological functions. These serum electrolyte levels are a reliable indicator of renal functions, and their determination can help administer proper renal disorders treatments. However, in the presence of kidney disorders, an unhealthy diet, and drugs or therapeutic agents that interfere with kidney functions, the kidney loses the ability to maintain average electrolyte balance. The significantly elevated serum sodium (Na^+), potassium (K^+), and chloride (Cl^-), together with the considerably depleted serum bicarbonate levels in the dutasteride control rats, are attributed to the toxic effects of Dutasteride on the kidney and decline in the functions of the rats following previous reports (6). The elevated serum Na^+, K^+, and Cl^- in the dutasteride control rats suggest the impaired ability of the kidney to filter and excrete excess serum Na^+, K^+, and Cl^- ions from the blood to maintain their optimum levels to enhance normal physiological and biochemical functions.

Moreover, the decreased serum bicarbonate ion levels in the dutasteride control showed that the rats had metabolic acid acidosis due to low bicarbonate ions to maintain acid-base balance, which aligns with Raphael *et al*. (6). Dutasteride induction in the rats made the kidneys unable to excrete titrable acid and ammonia nor carry out proper filtration and reabsorption of bicarbonate ions which would have ensured acid-base balance in the blood. Besides, the average serum Na^+, K^+, Cl^- and bicarbonate ion levels in the rats administered with 1000 *mg/kg of Aju Mbaise* extract only showed that *Aju Mbaise* extract does not pose any toxic effects on the kidney but suggests that it could promote optimal kidney functions. The dose-dependent significant reduction in the serum Na^+, K^+, and Cl^- along with the considerable rise in the serum bicarbonate ion levels in the Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract showed the nephroprotective properties of the *Aju Mbaise* extract against Dutasteride induced nephrotoxicity. These improvements in the serum electrolyte levels in the Dutasteride-induced rats treated with *Aju Mbaise* extract are attributed to the bioactivities of the phytoconstituents of the *Aju Mbaise* extract to restore the standard glomerular filtration and the ability of the proximal tubules of the kidneys to reabsorb some of the filtered electrolytes align with the findings reported by Navaneethan *et al*., (5). The improved serum Na^+, K^+, and Cl^- levels in the Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract could support normal biochemical and physiological functions and prevent complications associated with excess levels in the blood and align with the findings of Navaneethan *et al*. (5). Furthermore, the improved level of the serum bicarbonate ions suggests the kidneys of the Dutasteride-induced rats treated with 500 and 1000 *Aju Mbaise* extract were able to regulate acid-base and avoid metabolic acid and its health consequences.

The lipid profile encompasses all the lipid components found in the blood, including triacylglycerol (TAG), total cholesterol, high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), and very low-density lipoprotein-cholesterol (VLDL-C). Abnormal lipid profile occurs when there are low or high serum concentrations of the lipid components of the lipid profile outside the normal range and are an excellent pointer to underlying diseases, including kidney disease, cardiovascular disease, obesity, diabetes, and high blood pressure (31). The significantly elevated total serum cholesterol, TAG, LDL-C, and VLDL-C levels, together with a decreased level of HDL-C in the dutasteride control rats, showed the dyslipidaemia effects of the Dutasteride in the rats. The elevated total serum cholesterol, TAG, LDL-C, and VLDL-C in the rats predisposed the rats to increased risk of atherosclerosis, cardiovascular disease, stroke, and hypertension, which may worsen the kidney malfunctions in the rats aligns with Efremov *et al*. (32). The decreased HDL-C in the rats may not efficiently transport elevated serum LDL-C and VLDL-C levels to the liver for metabolism and, as such, could be deposited on the blood vessels, and high blood pressure affects the kidney, heart, and other organ functions. The hypercholesterolemia and increased serum TAG levels could accelerate obesity, impair carbohydrate metabolism and induce diabetes which may be related to the excess collection of fatty acids in the abdominal regions and insulin insensitivity which aligns with Mattar *et al*. (33).

In contrast, the dose-dependent significant rise in the serum HDL-C levels and significant decline in the total serum cholesterol, TAG, LDL-C, and VLDL-C concentrations in the rats administered with only 1000 *mg/kg of Aju Mbaise* extract, Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise* extract respectively relative to dutasteride control rats show the antihyperlipidemic effects of th*e Aju Mbaise*. These antihyperlipidemic effects of *Aju Mbaise* align with previous findings (34, 35). The increased HDL-C levels in the rats show that excess cholesterol, TAG, LDL-C, and VLDL-C will be rapidly transported to the liver for catabolism, thereby preventing their excessive accumulation in the body. The declined levels of LDL-C in the Dutasteride-induced rats treated with *Aju Mbaise* extract suggest that LDL-C accumulation and deposition of lipid droplets along the arterial wall are not like to occur. Thus, treating Dutasteride-induced rats with *Aju Mbaise* extract could reduce the risk of atherosclerosis, hypertension, cardiovascular diseases, and health complications of dyslipidaemia, in line with Se-Eun *et al*. (35). Treatment of Dutasteride-induced rats with *Aju Mbaise* extract could improve lipid and

carbohydrate metabolism, prevent excessive TAG deposition on the fatty tissues obesity, and reduce the accumulation of fats in the abdominal regions, promoting sensitivity of insulin receptors to the insulin secreted by the beta cells of the pancreas. This finding is consistent with the results of Anyanwagu *et al.* (36).

Evaluating the haematological components' status help diagnose and monitor the prognosis of various anaemia, blood clotting disorders, and infections, including haematological cancers. The significantly elevated WBC, Platelets, MCV, and lymphocyte levels, along with the decreased RBC, PCV, Hb, MCHC, and neutrophil levels in the dutasteride control rats indicated the toxic effects of Dutasteride on the rats in line with similar reports by Patrick-Iwuanyanwu and Nkpaa (37). The dutasteride control rats could have high levels of WBC and lymphocytes as an immunological response to the Dutasteride toxicity. Furthermore, the Dutasteride induction without treatment could induce an increased rate of RBC haemolysis and impair the ability of the haematopoietic cells to synthesize sufficient RBC that would counter the amount of RBC lost via haemolysis, and this could be responsible for the highly reduced RBC, PCV, Hb, and MCHC levels. These reductions in the RBC, PCV, Hb, and MCHC levels of the dutasteride control rats indicated that Dutasteride induction caused anaemic conditions in the rats and agreed with Bigoniya *et al*. (38). Moreover, the elevated platelet counts in the dutasteride control rats indicate an increased risk of blood clotting along the blood vessels, predisposing the rats to develop complications such as paralysis and cardiovascular disorder. The elevated RBC, PCV, Hb, MCV, MCH, MCHC, and neutrophil levels, together with the decline in the WBC, platelets, and lymphocytes counts of the rats administered with 1000 mg/kg of *Aju Mbaise* extract only showed that *Aju Mbaise* had no adverse effects on the haematological functions.

Similarly, the elevated RBC, PCV, Hb, MCV, MCH, MCHC, and neutrophil levels, along with the decline in the WBC, platelets, and lymphocytes counts of Dutasteride-induced rats treated with *Aju Mbaise* extract showed that *Aju Mbaise* extract was able to reverse the toxic effect of Dutasteride on haematological parameters consistent with the findings of Bigoniya *et al*. (38). The high levels of RBC, PCV, Hb, MCV, MCH, and MCHC suggest that *Aju Mbaise* extract prevented the rats from anaemia, unlike the dutasteride control rats that exhibited features of anaemia in their haematological indices, which is consistent with with the findings of Patrick-Iwuanyanwu and Nkpaa (37). Thus, *Aju Mbaise* extract could serve as a potent anti-anaemic agent, replenish blood loss through injury or during childbirth, and validate its use by nursing mothers immediately after birth and up to two months after delivery. Although low platelet counts could increase the risk of uncontrolled bleeding due to a decrease in blood clotting, the platelet counts observed in the Dutasteride-induced rats treated with *Aju Mbaise* extract were within the normal range relative to the sham control and would promote normal haematological functions. Similarly, the significant reduction in the WBC ad lymphocyte counts showed that *Aju Mbaise* extract could serve as an immune modulator as it was able to attenuate Dutasteride toxicity and restore normal immunological responses in the rats align with the reports of Patrick-Iwuanyanwu and Nkpaa (37).

The normal renal histo-morphologies observed in the dutasteride control, the rats administered with 1000 *mg/kg of Aju Mbaise* only, and Dutasteride-induced rats treated with 500 and 1000 *mg/kg of Aju Mbaise*, respectively, relative to the sham control showed that Dutasteride induction could have resulted to the impairment of renal functions instead of renal injury. The altered renal functions indicate that induction of renal injury may not be the primary mechanism of Dutasteride toxicity and impairment of renal function. Further studies are needed to understand how Dutasteride causes the impairment of renal functions in the rats. This finding is contrary to the result reported by Ogugua *et al.*, who worked with *Nauclea latifolia* and reported significant alterations in the kidney histology of Alloxan-induced diabetic rats (39).

Conclusion

The findings of this study indicated that the treatment of Dutasteride-induced rats with *Aju Mbaise* extract could replenish blood parameters to normal levels and attenuate renal injury and dyslipidaemia caused by Dutasteride toxicity in the rats. The *Aju Mbaise* extract had no adverse effects on the lipid profile, renal

function, and haematological parameters of the rats administered with a very high dose of *Aju Mbaise* extract without Dutasteride induction. The findings suggest that a high amount of *Aju Mbaise* extract possesses better nephroprotective, anti-dyslipidaemia, and blood replenishing properties than a low amount.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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